REMARKS/ARGUMENTS

Claims 10 and 12-21 were currently pending in the above-identified application and were examined. Claim 15 has been withdrawn from prosecution subsequent to a request for a species election by the Examiner. By the present response Claim 10 has been amended and new claims 36 through 43 have been added. Support for these amendments and new claims is identified in the following remarks. No new matter is added by the amendments and new claims. The prior rejections under 35 U.S.C. § 112, first paragraph, have been withdrawn.

Rejections under 35 U.S.C. §103(a)

Claims 10, 12-14 and 16-21 remain rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 5,788,963 (1998, IDS) in view of Ramoner *et al.* for the reasons of record as set forth in the action mailed September 25, 2003. In particular, the Examiner believes that Applicants' prior arguments regarding the instant inventor's reasons for administering antigen- and BCG-exposed DCs to a patient comprise only further characterization of a method made obvious by the prior art and that further characterization of a method does not render a method patentably distinct. In the present case, the Examiner believes that the secondary reference (Ramoner *et al.*) provides adequate motivation for exposing antigen loaded DCs to BCG for use in tumor therapy. The Examiner, in particular, states "as set forth in the reference, BCG had been used to treat tumors, BCG was known to stimulate DCs, and the authors even suggested the use of BCG with DCs in tumor immunotherapy.

Applicants do not agree with the Examiner's summary of the motivation provided by the disclosure of Ramoner *et al.* that Applicants have only provided further characterization of a method made obvious by the prior art. But, in order to further expedite prosecution of certain subject matter disclosed in the present application claim 10 has been amended to recite the present invention with greater particularity and new claims 36 through 43 have been added to recite specific embodiments of the invention disclosed in the application as filed, but not previously claimed. In particular, Claim 10 has been amended to recite "[a] method for

producing an antigen specific cytotoxic T cell response, comprising: administering, to a patient in need thereof, an effective amount of human dendritic cells, exposed *in vitro* to an antigen and bacillus Calmette Guerin (BCG) or BCG with lipopolysaccharide (LPS) to promote Major Histocompatibility Complex- (MHC-) class I processing of the antigen, such that after administration the human dendritic cells presenting the antigen in the context of MHC-class I elicit the antigen specific cytotoxic T cell immune response." As previously stated by Applicants Ramoner *et al.* do not disclose or suggest the use of BCG, or BCG and LPS, combined with an antigen can promote a MHC-class I response. This response is analogous to an antigen specific cytotoxic T cell response. Ramoner *et al.* only disclose that BCG induces a MHC-class II response in dendritic cells as measured by the proliferation of allogenic T cells. There is no suggestion or disclosure of a method for inducing an MHC-class I response. Applicants do not believe that this is the same invention or that the invention as presently claimed is merely further characterization of a method suggested by the cited art as suggested by the Examiner.

Ramoner *et al.* only suggest generally the use of BCG in dendritic cell based immunotherapy. There is no suggestion or detailed enablement of how BCG might be used, such as for example, combined with DCs at the time of administration or subsequent to administration as an adjuvant for an *in vivo* response, or in some other manner. The Examiner has suggested that Ramoner *et al.* provides motivation for "exposing antigen loaded DCs to BCG for use in immunotherapy." Applicants fail to see any motivation for this specific use of BCG as presently claimed way in Ramoner *et al.* and respectfully submit that the reference can be viewed as suggesting the *in vivo* use of BCG similar to its use in treating bladder cancer. It appears that the Examiner may be using the disclosure of the present invention in impermissible hindsight reconstruction of the pending claims.

Applicants have also added new claims 36 through 43. Claim 36 through 39 are added to specifically recite that the DCs administered to the patient were "exposed *in vitro* to an antigen and BCG or BCG and LPS" simultaneously. Support for this amendment can be found, for example, at page 29, lines 25 through 28. The antigen can be, for example, a lysate of cancer tumor cells isolated from a patient, a membrane preparation of tumor cells isolated from a

patient, a purified tumor specific antigen, a purified tumor associated antigen, a purified tissue associated antigen, a purified tissue specific antigen, or an antigenic fragment thereof, a prostate tumor associated antigen, a lysate of prostate tumor cells of a prostate cancer patient, a membrane preparation of prostate tumor cells of a prostate cancer patient, purified prostate specific membrane antigen (PSMA), a peptide having the amino acid sequence Leu Leu His Glu Thr Asp Ser Ala Val (SEQ ID NO. 1), a peptide having the amino acid sequence Ala Leu Phe Asp Ile Glu Ser Lys Val (SEQ ID NO. 2), a peptide having the amino acid sequence Xaa Leu (or Met) Xaa Xaa Xaa Xaa Xaa Xaa Val (or Leu) where Xaa represents any amino acid, purified prostate specific antigen (PSA), purified prostate acid phosphatase (PAP), six transmembrane epithelial antigen of the prostate (STEAP), prostate carcinoma tumor antigen (PCTA-1), prostate stem cell antigen (PSCA), or purified prostate mucus antigen recognized by monoclonal antibody PD41.

New claims 40 through 43 are added to specifically recite a method wherein the DCs administered to the patient are exposed *in vitro* to BCG, or BCG and LPS, prior to exposure to an antigen. Support for claim 40 through 43 can be found, for example, in Example 2 beginning at page 31, line 27. In this example it is demonstrated that the addition of BCG induces the maturation of immature dendritic cells as indicated by the increase in CD83 and HLA-class I. Further, contrary to the prior art the data demonstrates that although antigen uptake is reduced subsequent to exposure to BCG or BCG and LPS (indicated by the uptake of FITC dextran), a substantial amount of antigen is still taken in for processing. (See Table 2 and Table 3, at page 34). Applicants do not believe that either of these particular methods are disclosed or suggested by Ramoner *et al.*

Applicants do not believe that Ramoner *et al.* provide any motivation to combine DCs, an antigen and BCG in the manner recited in the pending claims. Further, Ramoner *et al.* neither alone or in combination with U.S. Patent 5,788,963 explicitly suggest the claim element that is the difference between the claimed invention and the prior art. Also, no detailed enabling methodology for practicing the claimed invention is disclosed, and there is no suggestion to modify the prior art to practice the invention as claimed. Still further, the references do not

provide any evidence suggesting that the invention as presently claimed would be successful. As such, Applicants do not believe that the invention as presently claimed is obvious over U.S. Patent 5,788,963 in view of Ramoner *et al.*. Therefore, reconsideration of the claims as amended and withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-467-9600.

Respectfully submitted,

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